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10/727,580	12/05/2003	Guy Sauvageau	14632-7 FC	7319

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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/727,580	SAUVAGEAU ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/29/2006, 10/2/2006, 7/10/2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *1-6,14-17,24 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-13 and 18-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 June 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/17/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-25 are pending in the instant application.

Election/Restrictions

Applicant's election with traverse of Group II in the reply filed on 6/29/2006 is acknowledged. Applicant's election with traverse of the species HOXB4 in the reply filed on 10/2/2006 is acknowledged. The traversal is on the ground(s) that groups I-IV are related to a product and process of using and that the process cannot be practiced with a materially different product. This is not found persuasive because restriction between products and processes of using the products is proper when it can be shown that the product as claimed can be used in a materially different process. Group II is drawn to a method of using Group I. As stated on page 3 of the Office action mailed 5/30/2006, the stem cell expansion factor of Group I can be used in a materially different process such as *in vitro* assays for protein or DNA binding.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-6, 14-17, 24 and 25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 6/29/2006.

An examination on the merits of claims 7-13 and 18-23 follows.

Information Disclosure Statement

Receipt of an information disclosure statement, filed on 8/17/2005, is acknowledged. The signed and initialed PTO 1449 has been mailed with this action.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below.

Figure 7A contains the TAT sequence of SEQ ID NO: 6; however, the sequence is not referred to by the use of a sequence identifier. Where the description or claims of a patent application discuss a sequence that is set forth in the Sequence Listing, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application. It would be remedial to amend the brief description of Figure 7A to include a reference to SEQ ID NO: 6.

In response to this office action, Applicant must comply with the sequence rules, 37 CFR 1.821 - 1.825. The nature of the non-compliance did not preclude an examination of the elected invention on the merits, the results of which are presented below.

Specification

The abstract of the disclosure is objected to because the phrase "may is" in the last sentence is not grammatically correct. It would be remedial to amend the last sentence of the abstract to delete the word "may." Correction is required. See MPEP § 608.01(b).

The disclosure is objected to because of the following informalities: at page 1, paragraph 1 the status of USSN 09/785,301 needs to be updated. The application is now abandoned.

Appropriate correction is required.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See page 55, lines 12-14 and 34.

Drawings

The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: element F of Figure 1 is not specifically described in the specification. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will

be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

Claims 8-13 and 19-23 objected to because of the following informalities: the claims refer to "a method" of a previous claim. To make it clear that the claim refers only to the method of the previous claim, it would be remedial to amend the claims to recite "the method" rather than "a method" in the first line of the claims. Appropriate correction is required.

Claims 7-13 and 18-23 are objected to because of the following informalities: the claims depend from withdrawn claims. Appropriate correction is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 7-13 and 18-23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 31-39, 43 and 44 of copending Application No. 10/530,413 (hereinafter the '413 application).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 7-13 and 18-23 are generic to all that is recited in claims 31-39, 43 and 44 of the '413 application. That is, claims 31-39, 43 and 44 of the '413 application fall entirely with the scope of claims 7-13 and 18-23 of the instant application or, in other words, instant claims 7-13 and 18-23 are anticipated by claims 31-39, 43 and 44 of the '413 application. The claims of the '413 application are narrower in scope than the instant claims in that they require the use of the product of claim 15 which comprises additional elements relative to the product of instant claim1. Specifically, the conflicting claims require the Hox peptide capable of crossing the cell membrane, and a blocker, which reduces the expression level of at least one gene normally limiting HOX-induced expansion of stem cells.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10, 11, 21 and 22 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "HIV-derived peptide" in claims 10, 11, 21 and 22 is a relative term that renders the claim indefinite. The term "HIV-derived peptide " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The term "HIV-derived peptide" is unclear in that one of ordinary skill in the art would not know how much one could vary the structure of the peptide in terms of amino acid sequence, for example, and meet the limitations of the claimed invention. It is unclear if "HIV-derived" means that the peptide was isolated from HIV, or whether the claims encompass peptides of different sequences. If the intent is to claim only peptides isolated from HIV, it would be remedial to amend the claim to recite "HIV peptide" or "a peptide isolated from HIV."

Claims 12 and 13 depend from claims 10 and 11 and thus are indefinite for the same reasons applied to claims 10 and 11.

Claim 13 is vague and indefinite in that the metes and bounds of the phrase "wherein said hematopoietic stem cell is human" are unclear. It is unclear if the claim is drawn to a human comprising a hematopoietic stem cell or whether the stem cell is isolated from a human. If the

latter meaning were intended, it would be remedial to amend the claim to recite, "wherein said hematopoietic stem cell is isolated from a human."

Claim 23 is vague and indefinite in that the metes and bounds of the phrase "wherein said hematopoietic stem cell is human" are unclear. It is unclear if the claim is drawn to a human comprising a hematopoietic stem cell or whether the stem cell is isolated from a human. If the latter meaning were intended, it would be remedial to amend the claim to recite, "wherein said hematopoietic stem cell is isolated from a human."

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7, 9-13, 18, and 20-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims encompass the provision of a genus of stem cell expansion factors. The stem cell expansion factors are defined by the claims as comprising an amino acid sequence having the expansion enhancement activity of a peptide encoded by a Hox nucleotide sequence enhancing expansion of a stem cell population, and wherein the factor is able to cross a cell membrane. The rejected claims thus comprise a genus of proteins that are defined by function:

(1) have the enhancement activity of a hox peptide, and (2) are capable of crossing the cell membrane.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof. The specification describes Hoxb4 as specifically enhancing the repopulation potential of hematopoietic stem cells without inducing leukemic transformation (e.g., page 6, lines 5-7). The specification describes Hoxa4 as providing a competitive advantage when repopulating hematopoietic cells (e.g., pages 54-59). The specification describes Hoxb3 as enhancing the production of γδ T-lymphocytes (e.g., page 6, lines 7-10). The specification describes Hoxa10 as enhancing the generation of megakaryocytic progenitors (e.g., page 6, lines 10-12). The specification describes the Hoxb3 and Hoxa10 as being unable to expand populations of $CD4^+CD8^+$ αβ thymocytes and monocytes, respectively. Thus, the hox proteins do not share the common property of enhancing all stem cell expansion. The effect of the hox protein on the expansion of a particular stem cell type is dependent upon the structures that diverge between the different hox proteins. The specification describes the homeodomain of HOXB4 as containing a homeodomain that is completely conserved with the region of the Antp homeodomain that provides the ability of the protein to transduce the cell membrane (e.g., page 7, ones 11-28). Further, the specification describes the use of protein transduction domains to allow the hox protein to cross the cell membrane (e.g., page 7, line 29 to page 9, line 2; pages 37-39).

Even if one accepts that the examples described in the specification meet the claim limitations of the rejected claims with regard to structure and function, the examples are only representative of a few full-length hox proteins that are capable of expanding a stem cell population. The prior art teaches that mammals have 38 hox genes that are found in four clusters (Largman et al, US Patent No. 5,837,507; e.g., column 2, lines 28-30). Largman et al suggest that some of the hox genes may play a role in leukemogenesis (e.g., column 7, lines 29-34). The proteins that induce leukemia rather than cell expansion would not be suitable for use in the presently claimed invention. The results are not necessarily predictive of which hox proteins will have the desired function. Even if a representative number of hox proteins have the desired effect, the specification and prior art do not provide guidance as to which domains within the hox proteins are sufficient to provide the claimed function, and the claims read on the administration of less than the full-length protein and sequences that have the same function but are not necessarily obtained from a hox protein. Thus, it is impossible for one to extrapolate from the few examples described herein those proteins that would necessarily meet the structural/functional characteristics of the rejected claims.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of proteins, and therefore conception is not

achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18USPQ2d 1016.

Given the very large genus of proteins encompassed by the rejected claims, and given the limited description provided by the prior art and specification with regard to specific domains or sequences required for stem cell expansion activity, the skilled artisan would not have been able to envision a sufficient number of specific embodiments that meet the functional limitations of the claims to describe the broadly claimed genus of proteins. Thus, there is no structural/functional basis provided by the prior art or instant specification for one of skill in the art to envision those proteins that satisfy the functional limitations of the claims with regard to stem cell expansion activity. Therefore, the skilled artisan would have reasonably concluded applicants were not in possession of the claimed invention for claims 7, 9-13, 18, and 20-22.

Claims 7, 9-13, 18, and 20-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for enhancing expansion of a stem cell population, the method comprising directly delivering to a stem cell population an effective amount of a HOXB4 protein conjugated to an HIV transactivating protein (TAT) protein transduction domain, does not reasonably provide enablement for fragments of any hox protein or full-length proteins not taught as having stem cell expansion activity. The specification does

not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention and breadth of claims: The claims are drawn to a method for enhancing a stem cell population by directly delivering an effective amount of a stem cell expansion factor that comprises an amino acid sequence having expansion enhancement activity of a peptide encoded by a Hox nucleotide sequence enhancing expansion of a stem cell population, and wherein the factor is able to cross the cell membrane. The nature of the invention is complex in that the factor that is administered to the cells must be capable of expanding a stem cell population. The claims are very broad in that the factor is defined only by function and is not limited to a particular structure. The breadth of the claims greatly exacerbates the complex nature of the invention.

Guidance of the specification and existence of working examples: The specification teaches that Hoxb4 specifically enhances the repopulation potential of hematopoietic stem cells without inducing leukemic transformation (e.g., page 6, lines 5-7). The specification teaches that hoxa4 -/+ cells are unable to compete with hoxa4 +/+ cells for long-term repopulation of hematopoietic cells (e.g., pages 54-59). The specification teaches that Hoxb3 enhances the production of γδ T-lymphocytes (e.g., page 6, lines 7-10). The specification teaches that Hoxa10

enhances the generation of megakaryocytic progenitors (e.g., page 6, lines 10-12). The specification teaches that Hoxb3 and Hoxa10 are unable to expand populations of $CD4^+CD8^+$ αβ thymocytes and monocytes, respectively. Thus, the hox proteins do not share the common property of enhancing all stem cell expansion. The effect of hox protein on the expansion of a particular stem cell type is dependent upon the structures that diverge between the different hox proteins.

With regard to crossing the cell membrane, the specification describes the homeodomain of HOXB4 as containing a homeodomain that is completely conserved with the region of the Antp homeodomain that provides the ability of the protein to transduce the cell membrane (e.g., page 7, ones 11-28). Further, the specification describes the use of protein transduction domains to allow the hox protein to cross the cell membrane (e.g., page 7, line 29 to page 9, line 2; pages 37-39).

The working examples of the specification demonstrate that HOXB4-TAT protein is capable of expanding hematopoietic stem cells without affecting differentiation (e.g., pages 45-54). The specification does not provide working examples for other Hox proteins or proteins that have hox expansion activity.

The specification does not provide guidance as to which domains within the hox proteins are sufficient to provide the claimed function, and the claims read on the administration of less than the full-length protein as well as sequences that have the same function but are not necessarily obtained from a hox protein.

Predictability and state of the art: The prior art teaches that mammals have 38 hox genes that are found in four clusters (Largman et al, US Patent No. 5,837,507; e.g., column 2, lines 28-

30). Largman et al suggest that some of the hox genes may play a role in leukemogenesis (e.g., column 7, lines 29-34). The proteins that induce leukemia rather than cell expansion would not be suitable for use in the presently claimed invention.

Amount of experimentation necessary: The claims encompass the provision of a genus of proteins that are defined only by their function, where the relationship between the structural features of the members of the genus and the claimed function has not been defined. In the absence of such a relationship either disclosed in the as-filed application or which would have been recognized based upon information readily available to one skilled in the art, the skilled artisan would not know how to make the proteins that lack structural definition. The fact that one could assay each protein for activity in the claimed method does not overcome this defect since one would have no knowledge beforehand as to whether or not any given protein sequence (other than those specifically disclosed in the present specification) would fall within the scope of what is claimed. It would be an undue burden to randomly screen undefined proteins for the claimed activity.

In view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, the skilled artisan would have required an undue amount of experimentation to make the claimed invention. Therefore, claims 7, 9-13, 18, and 20-22 are not considered to be fully enabled by the instant specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7-13 and 18-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Largman et al (US Patent No. 5,837,507, cited on the IDS filed 8/17/2005) in view of Frankel et al (US Patent No. 5,804,604; see the entire reference).

Largman et al teach the expression of an exogenous HOX gene, preferably HOXB4, in a stem cell to generate expanded population of pluripotent stem cells *in vitro* or *in vivo* (e.g., Abstract; column 2, lines 35-59; column 8, lines 5-38; column 11, line 53 to column 12, line 50). The preferred stem cell is a hematopoietic stem cell, such as a human hematopoietic stem cell expressing the cell surface marker CD34 (e.g., column 2, lines 48-59). Largman et al teach that it is the expression of the HOXB4 gene (i.e., the HOXB4 protein) that results in the desired function (e.g., column 12, lines 5-37).

Largman et al do not teach the method where the HOXB4 protein is delivered to the stem cell by crossing the cell membrane as a result of the presence of a HIV-TAT protein.

Frankel et al teach the delivery of biologically active proteins to the cytoplasm and nuclei of cells *in vitro* and *in vivo* by the u se of transport polypeptides which comprise HIV tat protein, which are covalently attached to the cargo protein (e.g., Abstract; column 1, lines 20-40; column 2, line 64 to column 4, line 3; column 7, lines 23-38). Frankel specifically teach the delivery of a transcription factor by TAT mediated protein transduction (e.g., column 12, lines 25-40). Further, Frankel et al teach that methods of DNA delivery typically deliver the nucleic acid molecules into only a fraction of the total cell population and tend to damage large numbers of cells (e.g., column 1, lines 54-63). In contrast, the methods of using the tat protein to deliver

proteins provide efficient delivery of non-tat proteins that are not inherently capable of entering target cells or nuclei, or are not inherently capable of entering cells at a useful rate (e.g., column 3, lines 6-15).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of generating expanded populations of stem cells of Largman et al to replace the delivery of HOXB4 protein by delivering a nucleic acid molecule with the delivery of HOXB4 protein by delivering a tat-conjugated protein as taught by Frankel et al because Largman et al teach it is within the ordinary skill in the art to use HOXB4 protein expression to expand populations of stem cells and Frankel et al teach the delivery of proteins to cells *in vitro* and *in vivo*.

One would have been motivated to make such a modification in order to receive the expected benefit of more efficiently delivering the HOXB4 protein to the nucleus of the cells as taught by Frankel et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached at 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

/JD/

CELINE QIAN, PH.D.
PRIMARY EXAMINER